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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/784,673	02/24/2004	Louise Edwards	2931-219	1883

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EXAMINER	
MCKENZIE, THOMAS C	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 05/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/784,673	EDWARDS ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 16-18* is/are rejected.

7)☒ Claim(s) *15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to an application filed on 2/24/04. There are eighteen claims pending and eighteen under consideration. Claims 1-15 are compound claims. Claim 16 is a composition claim. Claims 17 and 18 are method of using claims. This is the first action on the merits. The application concerns some 6-aminoalkyindole and indazole compounds, compositions, and uses thereof.

Priority

2. The status of non-provisional parent application should also be included. Since the parent application has become a patent, please update the first line of the specification with the expression "now Patent No. 6,716,837" following the filing date of the parent application.

Title

3. The title of the invention is no longer descriptive after restriction. A new title is required that is clearly indicative of the invention to which the claims are directed. The following is suggested: replacing "Heterocyclic Compounds" by "6-Aminoalkyindole and Indazole ".

Abstract

4. Applicant is reminded of the proper content of an abstract of the disclosure. A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. In chemical patent abstracts for compounds or compositions, the general nature of the

compound or composition should be given as well as its use, *e.g.*, "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." The abstract is too short and generic. Examiner suggests claim 1, lines 1-16, including the figure, and the utility.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 10-13, and 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "such that A contains at least 1 N atom" is confusing. Formula II, which is A, already contains one mandatory nitrogen atom. Is the "1 N atom", referred to above, in addition to this mandatory nitrogen? That is must radicals R_2 and/or R_3 also contain a nitrogen atom? Or does the "1 N atom" refer to the nitrogen atom pictured in Formula II. If the latter, the Examiner suggests removing the phrase.

6. Claims 1-8, 10-13, and 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The variable "h"

is not defined in the claims. The Examiner suggests relying upon line 1, page 3 to claim h = 2-3 and that is what was searched.

7. Claims 1, 8-13, and 15-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation "alkyl" in the definition of radical R_1, and the claim also recites "including C(1-12)alkyl" which is the narrower statement

of the range/limitation. The Examiner suggests deleting the phrase "alkyl including".

8. Claims 1, 8-13, and 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The word "heterocycloalkylalkenyl", in the definition of radical R_1 is indefinite. There is no such thing. Is it an alkyl substituted by a heterocycle and in turn substituted by an alkenyl, e.g. pyridyl-methylvinyl? A cycloalkyl interrupted by a heteroatom and substituted by an alkenyl, such as vinylpiperidinyl? A cycloalkyl substituted by a heteroatom, which in turn is substituted by an alkenyl, e.g. chlorocyclohexylvinyl? Whatever choice is selected must be supported by the specification.

9. Claims 1-7, 10-13, and 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the definition of CR_5 it is unclear if the five different choices for this diradical can be made independently. If h = 2 and one of the CR_5 groups is CH_2, then must the second be CH_2 or can it be one of the other possibilities? Applicants can address this question in connection with the art rejection over Brown ('386) made below.

10. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 8 recites the limitation "N-cycloalkyl" in line 2. There is no antecedent basis for this limitation in the parent claim 1. The A group requires some kind of alkylenyl chain linking the heterocyclic nucleolus to the nitrogen atom.

11. Claims 10 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 10 recites the limitation "indoline" in line 2. There is no antecedent basis for this limitation in the parent claim 1. Claim 1 contains formula I, which has a double bond between atoms W and Z in the five-membered ring. An indoline has a saturated five-membered ring, lacking this mandatory double bond. The Examiner suggests deleting the term "indoline".

12. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining what is a "medical condition for which stimulation of 5-HT_{1D} receptor

is indicated". It is unclear which diseases require "stimulation of 5-HT_{1D} receptor"? The 5-HT_{1D} receptor is discussed in the second paragraph on page 25 of "Annual Reports in Medicinal Chemistry, Vol. 27", cite AG and the only disease mentioned is migraine.

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 and 16-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using compounds of Formula I with B = D = CH and Z = C, does not reasonably provide enablement for using compounds with nitrogen atoms at any of these positions. The specification is not adequately enabled for the scope of fused rings that have diverse atoms at both the six and five membered rings. Compounds made and tested represent the scope of claim 12, not claim 1. The specification does not enable any skilled pharmacologist or physician to use the invention commensurate in scope with these claims. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re*

Rainer, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546.

a) Determining if any particular claimed compounds with nitrogen any of positions B, D, and Z would be active would require synthesis of the substrate and subjecting it to testing with Applicants' *in vitro* assay. Considering the large number of compounds to be made this is a large quantity of experimentation. b) The direction concerning the claimed fused pyridine, triazole, and imidazole compounds is found in lines 12-14, page 2, which merely states Applicants intent to make and use such compounds. c) In the instant case none of the working examples contains any fused pyridine, triazole, and imidazole cores. None of these working examples contain a basic atom in the six-membered ring. None of these contain electron deficient hetero aromatic rings as the six-membered ring. d) The nature of the invention is inhibition of 5-HT_{1B} receptor and treatment of human diseases with Applicants' compounds. This involves physiological activity. The nature of the invention requires an understanding of the 5-HT_{1B} receptor, the binding activity of small ligands to that receptor, and the ability of those compounds to treat migraines. In view of the unpredictability of receptor binding activity and claimed divergent substituents with varied polarity, size, and polarisability, the skilled physician would indeed question the inclusion of such

diverse rings, commensurate in scope with these claims. Also see the MPEP § 2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry. e) The state of the art is detailed knowledge of the 5-HT_{1B} receptor is lacking. No X-ray structure of the receptor is known and the structural requirements of ligands to this receptor are poorly understood. The six-membered benzene ring of Applicants' working example benzimidazole compounds is non-basic. The pyridine ring and the pyrazine ring of the rejected compounds are weakly basic and strongly basic respectively. The pyridine ring and the pyrazine ring of the rejected compounds are hydrogen bond acceptors. The benzene ring of Applicants working examples is not. The pyridine ring and the pyrazine ring of the rejected compounds are π-electron deficient. The benzene ring of Applicants working examples is not. There is no reasonable basis for the assumption that the myriad of compounds embraced the present formula (I) will all share the same biological properties. For example, the rings include imidazoles with extra basic sites. The rings include pyridines with additional polarizable nitrogen atoms. The diverse claimed fused heteroaryl rings are chemically non-equivalent and there is no basis in the prior art for assuming in the non-predictable art of CNS pharmacology that structurally dissimilar compounds

will have such activity, *In re Surrey* 151 USPQ 724. Compounds made and tested represent the scope of claim 11 not claim 1.

f) The artisan using Applicants invention to treat diseases with the claimed compounds would be a physician with a MD degree and several years of experience. He would be unaware of how to predict *a priori* how a changing a heterocyclic ring would affect biological activity. In view of the divergent rings with varied basicity, steric hindrance, and polarisability, the skilled physician would indeed question the inclusion of such fused rings, commensurate in scope with these claims. g) Physiological activity, is well-known to be unpredictable, *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). h) The breadth of the claims includes all of millions of compounds of formula (I). Thus, the scope is very broad.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue

experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

14. Secondly, Applicants have not shown in the specification how to make these other heterocyclic compounds. In lines 2-19, page 23 there are synthetic schemes showing how to make imidazole and triazole compounds (scheme 9) and pyridine fused to pyrrole compounds (schemes 10 and 11). There is no guidance to how to make pyridine fused to pyrazoles, imidazoles, or triazoles, which are presently claimed. Scheme 9 shows how to make a bromine containing intermediate but does not show how to make the final compound of formula I with the "A" radical attached. Schemes 10 and 11 show the conversion of some radical X to the side chain "A" but offer no reagents or conditions to accomplish this task. Scheme 10 and 11 merely refer back to other such conversions using indole compounds. There are no working examples of the synthesis of any compound with nitrogen any of positions B, D, and Z.

15. Claims 1-13 and 16-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making solvates of the claimed compounds. The specification does not enable any person skilled in the

art of synthetic organic chemistry to make the invention commensurate in scope with these claims. The factors to be considered in making an enablement rejection have been summarized above. In the present case the important factors leading to a conclusion of undue experimentation are the absence of any working example of a formed solvate, the lack of predictability in the art, and the broad scope of the claims.

c) There is no working example of any solvate formed. The claims are drawn to solvates, yet the numerous examples presented all failed to produce a solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly.

g) The state of the art is that is not predictable whether solvates will form or what their composition will be. In the language of the physical chemist, a solvate

of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry, cite AU). The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, "it is not usually possible to predict whether solid solutions will form, or if they do form what is their compositional extent". Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometery of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. In the same paragraph on page 365 West (Solid State Chemistry) explains that it is possible to make meta-stable non-equilibrium solvates, further clouding what Applicants mean by the word solvate. Compared with polymorphs, there is an additional degree of freedom to solvates, which means a different solvent or even the moisture of the air that might change the stabile region of the solvate.

h) The breadth of the claims includes all of the hundreds of thousands of compounds of formula I as well as the presently unknown list of solvents embraced by the term "solvate". Thus, the scope is broad.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the

time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

16. Claim 17 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating migraines, does not reasonably provide enablement for treating every "medical condition for which stimulation of 5-HT_{1D} receptor is indicated". The specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The how to make requirement of the enablement statute, when applied to process claims, refers to operability and how to make the claimed process work. The factors to be considered in making an enablement rejection have been summarized above. The three main issues are the lack of any correlation between clinical efficacy for disease treatment and Applicants' two *in vitro* assays, the state of the prior art, and the breadth of the claims.

There is an *in vitro* assay, drawn to binding to the 5-HT_{1B} and H-HT_{1D}, receptors described in lines 1-28, page 55 with data on 12 compounds. Applicants do not state and it is not recognized in the CNS therapeutic arts this assay is

correlated to clinical efficacy for the treatment of diseases. The state of the clinical arts in 5-HT_{1D} receptor pharmacology is discussed in the second paragraph on page 25 of "Annual Reports in Medicinal Chemistry, Vol. 27" and the only disease mentioned is migraine.

The scope of the claims involves all of the thousands of compounds of claim 1 as well as the unknown number of diseases embraced by the term "medical condition for which stimulation of 5-HT_{1D} receptor is indicated". Thus, the scope of claims is very broad.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

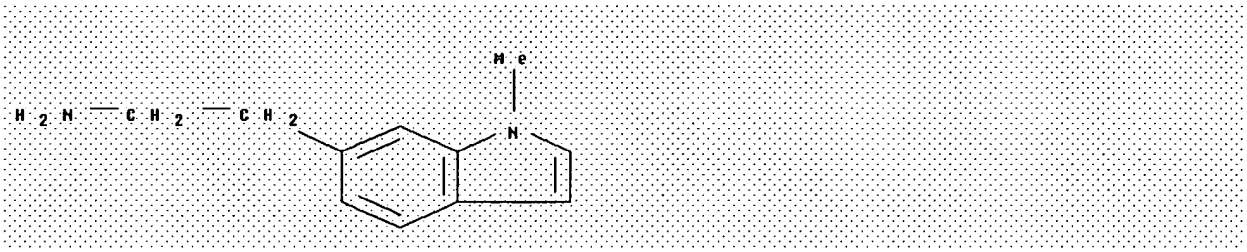
Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

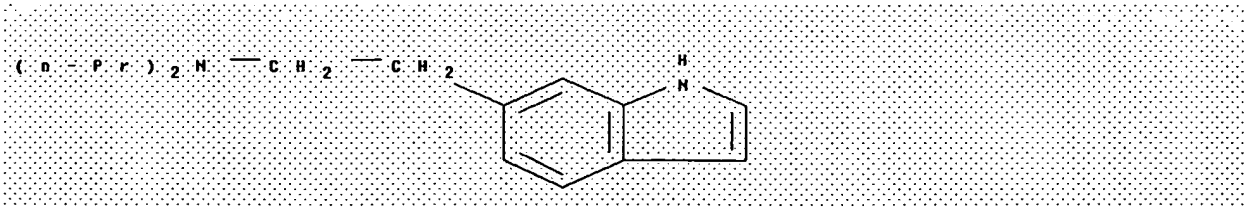
> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

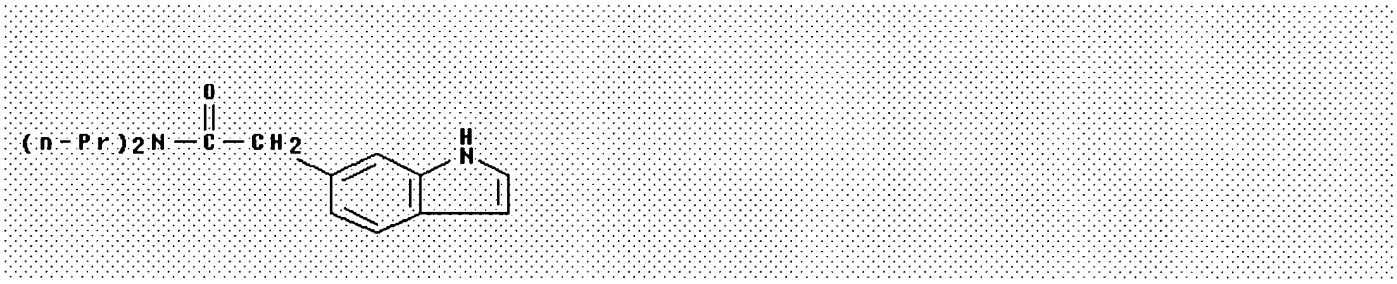
Claims 1, 6, and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Naruto (Chem. Pharm. Bull., cite AN). The compound with registry number 74631-89-3 and shown below fits Formula I with R_1 = methyl, W = B = D = CH, Z = C, $CR_5 = CH_2$, $R_2 = R_3 = R_4$ = H, and h = 2 meet the limitation of these claims. The compound can be found in the fourth paragraph on page 907 as compound 8.



18. Claims 1, 8, and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Nichols (J. Med. Chem., cite AO). The compound with registry number 122519-98-6 and shown below is of Formula I with $R_1 = R_5$ = H, $R_2 = R_3$ = propyl, W = B = D = CH, Z = C, $CR_5 = CH_2$, and h = 2 meet the limitation of these claims. The compound can be found as compound 4 in the paragraph spanning pages 2131 to 2132.



19. Claims 1, 8, 10-13, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Brown ('386, cite AA). The compound with registry number 21005-63-0 and shown below is of Formula I with $R_1 = R_4 = R_6 = H$, one $CR_5 = CO$, one $CR_5 = CH_2$, W = B = D = CH, Z = C, $R_2 = R_3$ = propyl, and h = 2 meet the limitation of these claims. The compound can be found in lines 5-28, column 21. See also claim 6 of this reference. Other examples are in part a, Examples 1-11. Claim 11 of this reference teaches compositions. Thus, the present claim 16 is anticipated.



Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nichols (J. Med. Chem., cite AO) as applied to claims 1, 8, and 11-13 above. The prior art teaches a compound with $R_2 = R_3$ = n-propyl. Applicants claim a compound with

$R_2 = R_3$ = i-propyl. The difference between the taught and claimed compounds is propyl side chain is branched rather than linear. Such structural isomers are *prima facie* obvious. The structural isomer is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing the isomers. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the isomers are obvious even in the absence of a specific teaching to rearrange the chain. See *In re FINLEY,* 81 USPQ 383, which found a *prima facia* case of obviousness of 2-ethyl hexyl salicylate over octyl salicylate taught in the prior art, *In re Hass* 60 USPQ 552, which found a *prima facia* case of obviousness of 1-chloro-1-nitrobutane over 1-chloro-1-nitroisobutane taught in the prior art, and *In re Wilder*, 195 USPQ 426, which found a *prima facia* case of obviousness of a 1,4-dimethylpentyl amine over a 1-methylhexyl amine taught in the prior art.

21. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nichols (J. Med. Chem., cite AO) as applied to claims 1, 8, and 11-13 above. The prior art teaches a compound with $R_2 = R_3$ = n-propyl. Applicants claim a compound with $R_2 = R_3$ = ethyl. The difference between the taught and claimed compounds is removal of a methylene from each propyl side chain. Compounds that differ only by the presence or absence of an extra methylene group or two are

homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologues. The homologue is expected to be prepared by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methylene groups. See *In re Wood,* 199 USPQ 137; *In re Hoke*, 195 USPQ 148, *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Fauque*, 121 USPQ; *In re Druey*, 138 USPQ 39.

Allowable Subject Matter

22. Claim 15 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

23. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-

direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

24. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (571) 272-0670. The FAX number for amendments is (571) 273-8300. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 9:00am to 5:30pm, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact James O. Wilson, acting SPE of Art Unit 1624, at (571)-272-0661.

Thomas C. McKenzie, Ph.D.
Primary Examiner
Art Unit 1624
(571) 272-0670

TCMcK/me